REMARKS

Restriction requirement

Applicants maintain that the restriction requirement should be withdrawn in that all claims were previously examined and allowed on September 5, 2002. A restriction at this late stage in prosecution requires approval from the Technology Center director and an express waiver of the requirement that the elected invention has not been examined to permit applicant to file a divisional application for the non-elected inventions.

See http://www.uspto.gov/web/offices/pac/dapp/opla/presentation/clmcontfinalrule.html, Frequently asked questions, pages 13-14.

Applicants also traverse the restriction requirement as without basis in that the seven inventions are classified in the same class and subclass and the alleged distinctions between the inventions (etiologies, symptoms and treatment regimens of the diseases) do not pertain to any claim element.

Furthermore, the Examiner has required restriction within a single claim. Applicants respectfully submit that 35 U.S.C. § 121 does not permit restriction within a single claim as clearly indicated by the Court in *In re Weber et al.* 198 USPQ 328 (1978).

> As a general proposition, an Applicant has a right to have each claim examined on the merits. If an Applicant submits a number of claims, it may well be that pursuant to a proper restriction requirement, those claims will be disbursed to a number of applications. Such action should not affect the right of the Applicant eventually to have each of the claims examined in the form he considers to best define his invention. If however a single claim is required to be divided up and presented in several applications, that claim would never be considered on its merits.
>
> It is apparent that §121 provides the commissioner the authority to promulgate rules designed to restrict an application to one of several claimed inventions when these inventions are found to be "independent and distinct." It does not however provide a basis for an Examiner acting under the authority of the Commissioner to reject a particular claim on that basis.

The Restriction Requirement in the above-identified application dated May 10, 2007, is

exactly the action that the Court *In re Weber* stated was not permitted under 35 U.S.C. §121. Such action by an Examiner would violate the "basic right of an Applicant to claim his invention as he chooses," since claim 1 does not actually recite the separate diseases identified in the seven groups.

New Claim 58

New Claim 58 has been added to provide a claim directed only to the elected subject matter.

Rejection Under 35 USC §112 , first paragraph

Applicants traverse the rejection of Claims 1-4(in-part) 28-34 (in-part) 38, 42-51(in part) and 54-55 (in-part) under 35 USC § 112, first paragraph, based on the allegation that the specification does not provide reasonable enablement for the elected subject mater.

The specification provides a number of publications which have linked TNFα production and/or signaling to a number of diseases including rheumatoid arthritis and many other inflammatory diseases or have linked diseases such as rheumatoid arthritis to excess or undesired matrix-destroying metalloprotease (MMP) activity.

The specification also discloses that inhibitors of p38 are active in animal models of TNFα production, including a murine lipopolysaccharide (LPS) model of TNFα production, in the text on page 5 of the specification which follows:

> Inhibitors of p38 are active in a number of standard animal models of inflammatory diseases, including carrageenan-induced edema in the rat paw, arachadonic acid-induced edema in the rat paw, arachadonic acid-induced peritonitis in the mouse, fetal rat long bone resorption, murine type II collagen-induced arthritis, and Fruend's adjuvant-induced arthritis in the rat. Thus, inhibitors of p38 will be useful in treating diseases mediated by one or more of the above-mentioned cytokines and/or proteolytic enzymes.

The specification also indicates that because inhibition of p38 leads to inhibition of MMP production and inhibition of TNFα production, p38 inhibitors (such as those of formula I) will be useful in treatment of the above listed diseases.

It is alleged that there is no link to the inhibition of TNFα (p38 inhibitors) and the treatment of the disease (rheumatoid arthritis). However, animal models such as those discussed in the application and disclosed by Badger et al. JPET 279:1453-1461(1996) (Exhibit A), do show such a link.(Badger et al. disclose the performance of SB 203580, a p38 kinase inhibitor, in animal models,

see Figs 3 and 6).

No evidence has been presented to refute the findings or conclusions made in these publications. In addition, no evidence has been presented that any of the methods claimed would not be effective in treating rheumatoid arthritis or any of the other p38 mediated diseases identified in the specification. Only unsupported allegations and conclusions regarding the state of the art are provided.

In any event, the specification also otherwise provides ample guidance as to how to prepare pharmaceutical compositions with the compounds of Formula I used in the claimed methods and how to administer these compositions in the treatment of rheumatoid arthritis and other p38 mediated diseases,(see, e.g., pages 24-29). The specification also provides dosage ranges for the various methods of administration (see, e.g., page 29). Given the extent of the disclosure provided, it would at most involve routine experimentation if any at all, for one of ordinary skill in the art to treat rheumatoid arthritis or any other p-38 mediated disease.

Even absent the specification disclosures discussed above, the rejection is clearly deficient in general under controlling case law. The courts have placed the burden upon the PTO to provide evidence shedding doubt on the disclosure that the invention can be made and used as stated; see, e.g., *In re Marzocchi*, 439 F.2d 220, 169 U.S.P.Q. 367 (CCPA 1971) (holding that how an enablement teaching is set forth, either by use of illustrative examples or by broad terminology, is of no importance.) The disclosure must be taken as in compliance with the enablement requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein. See *In re Marzocchi*, supra. No such evidence or reason for doubting Applicants' disclosure has been provided. Only general statements and conclusions are made.

Additionally, "the [enablement] requirement is satisfied if, given what they [, those of ordinary skill in the art,] already know, the specification teaches those in the art enough that they can make and use the claimed invention without 'undue experimentation.'" See *Amgen v Hoechst Marion Roussel*, 314 F.2d 1313, 65 USPQ2d 1385 (Fed. Cir. 2003). Using the compounds of formula I in the claimed methods would be routine for those of ordinary skill in the art in view of applicant's disclosure. Explicitly providing dedicated assays for each p38 mediated disease is not necessary to enable the methods claimed. See, for example, *In re Howarth*, 654 F.2d 105, 210 U.S.P.Q. 689 (CCPA 1981) ("An inventor need not ... explain every detail since he is speaking to

those skilled in the art."); *In re Gay*, 309 F.2d 769, 774, 135 U.S.P.Q 311 (CCPA 1962) ("Not every last detail is to be described, else patent specifications would turn into production specifications, which they were never intended to be.")

There is no requirement that an applicant provide any working examples relating to the treatment of every claimed disease to satisfy the statute. See, for example, *In re Angstadt*, 537 F.2d at 502-03, 190 USPQ 214 (CCPA 1976) (deciding that applicants "are *not* required to disclose *every* species encompassed by their claims even in an unpredictable art"); *Utter v Higara*, 845 F.2d at 998-99, 6 USPQ2d 1714 (Fed. Cir. 1988) (holding that a specification may, within the meaning of Section 112, Para. 1, enable a broadly claimed invention without describing all species that claim encompasses). Instead, as discussed earlier, there is no requirement for any examples. See, for example, *Marzocchi*, supra, stating that how "an enabling teaching is set forth, either by use of illustrative examples or by broad terminology, is of no importance." The MPEP also agrees by stating that "compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, does not turn on whether an example is disclosed." See MPEP § 2164.02.

The PTO has failed to meet its burden of establishing that the disclosure does not enable one skilled in the art to perform the methods claimed. Instead of relying on proper probative evidence, the rejection is improperly based on bare allegations and conclusions. No evidence has been presented which would demonstrate that the guidance provided by the specification is inadequate to enable the use of the claimed methods without undue experimentation.

As discussed in Wands, cited by the Examiner, "considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." Moreover, with respect to pharmaceutical inventions, an applicant is not required to test the claimed compounds in their final use (rigorous planned and executed clinical trials..." per the Examiner). The Federal Circuit in *In re Brana*, 51 F.3d 1560, 34 USPQ 1436 (Fed. Cir. 1995), stated that:

> usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful can be well before it is ready to be administered to humans. If the courts were to require

> Phase II testing in order to prove utility for pharmaceutical inventions, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas.

Here, the specification provides more than it needs to, e.g., *in vitro* raf kinase assays (and IC_{50} data) and *in vivo* assays (see pages 103 and 104). In similar fashion, one of ordinary skill in the art by performing the same or similar tests, can, by routine experimentation, determine the activity levels of each of the claimed compounds in treating rheumatoid arthritis and other p38 mediated diseases. This is absolutely routine in the field.

Thus, appellants have provided more than adequate guidance (and examples) to enable the claimed invention.

For the reasons discussed above, Applicants submit that all pending claims meet the requirements of 35 U.S.C.§ 112, first paragraph.

No fee is believed to be due with this response, however, the Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

/Richard J. Traverso/

Richard J. Traverso, Reg. No. 30,595
Attorney/Agents for Applicant(s)

MILLEN, WHITE, ZELANO
& BRANIGAN, P.C.
Arlington Courthouse Plaza 1, Suite 1400
2200 Clarendon Boulevard
Arlington, Virginia 22201
Telephone: (703) 243-6333
Facsimile: (703) 243-6410
Attorney Docket No.: BAYER-0011-C01
Date: October 29, 2007